



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES,  
AND  
TOXIC SUBSTANCES

**DATE:** August 31, 2001

**SUBJECT:** **Propanil.** The Outcome of the HED Metabolism Assessment Review Committee to discuss degradates in drinking water on August 7, 2001. PC code 028201; Rereg. Case 0226; DP Barcode: D277494.

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**THROUGH:** Al Nielson, Branch Senior Scientist  
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and  
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Reregistration Branch I  
Health Effects Division (7509C)

**TO:** Yan W. Donovan, Chemist,  
MARC Executive Secretary  
Registration Action Branch I  
Health Effects Division (7509C)

### Material Reviewed

The Metabolism Assessment Review Committee (MARC) met on August 7, 2001 to consider the degradation of propanil [3,4-dichloropropionanilide] in water. Specifically, MARC was asked to determine which degradates should be included in the risk assessment. The Environmental Fate and Economics Division (EFED) provided information that was presented to MARC (Ibrahim Abdel-Saheb) describing degradates found or having the potential to be found in soil and water.

### MARC Conclusions

The Committee concluded that parent and the metabolite 3,4-dichloroaniline (3,4-DCA) should be included in risk assessment. EFED should provide their best estimates of these residues in drinking water for chronic risk assessment. The impurity TCAB need not be included in the risk assessment unless EFED finds TCAB at detectable levels in monitoring data. The maximum level of this moiety in the fate studies was 0.5% of the total activity.

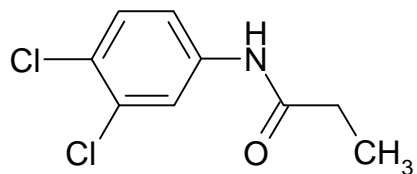
## Supporting Reasons

The Committee considered the following information to arrive at the conclusion shown above:

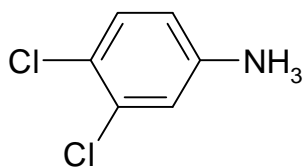
- The major degradate observed in guideline soil and water studies was 3,4-DCA. Minor degradates identified in aerobic soil metabolism and aerobic aquatic metabolism studies were TCAB and DCAB. The degradates TCAB and DCAB are not likely to be found in drinking water at detectable levels: (1) in laboratory and field the degradates TCAB and DCAB were found at 0.5% in the aerobic aquatic metabolism study and DCAB was found to <10% in the aerobic soil metabolism study (2) in monitoring data, these degradates were not found. Available monitoring data identified the major degradate as 3,4-DCA.

- Although no mechanistic studies have been submitted to the agency, open literature publications addressed the mode of action of propanil. Methemoglobinemia is the principal toxicological effect of concern for propanil. The ability of propanil and its metabolites to induce methemoglobinemia was evaluated in both *in vitro* and *in vivo* experiments. Using a rat microsome preparation, propanil was metabolized to 3,4-dichloroaniline (DCA) via acrylamidase-catalyzed hydrolysis; 2'-hydroxy-3,4-dichloroaniline (N-OH-DCA) and 6-hydroxy-3,4-dichloroaniline (6-OH-DCA) were also identified. Of these three metabolites, N-OH DCA and 6-OH DCA produced methemoglobin in a dose-dependent manner in rat RBC suspensions. Of the two methemoglobin-inducing metabolites, N-OH-DCA was at least 10 times greater than 6-OH-DCA. Following propanil administration (1.0 mmole/kg (218 mg/kg) to rats showed that both dichloroaniline and N-hydroxy-3,4-dichloroaniline were found in the blood.

**Figure 1:** Propanil and Degradates:

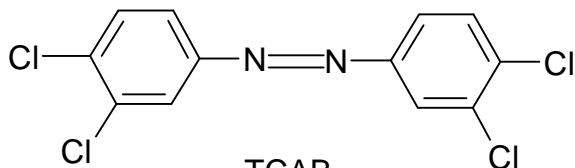


Propanil



DCA

3,4-dichloroaniline



TCAB

Bis(3,4-dichlorophenyl)diazene

## Individuals in Attendance

### 1. MARC Members:

Richard Loranger , Yan Donovan, Abdallah Khasawinah, Thuy Nguyen, Leung Cheng, George Kramer (alternate), William Dykstra (alternate), and Sheila Piper.

### 2. Scientists (non-MARC members)

Sherrie Kinard, Susan Makris, Ibrahim Abdel-Saheb, and Shana Recore.

cc: SF, RF, List A File, S.Kinard (RRB2), S. Makris (TOX), Ibrahim Abdel-Saheb (EFED)

RDI: C.Olinger: 8/15/01; A. Nielson: 8/31/01

7509C: RRB2: S. Kinard: CM#2:Rm 722B: 703-305-0563: 8/31/2001.